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Incidence Patterns of Lyme Disease and Cutaneous B-Cell Non-Hodgkin's Lymphoma in the United States

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Key Words
Lyme disease · Cutaneous B-cell lymphoma · Geographic correlation

Abstract
Background: Several reports have suggested a link between infection with *Borrelia burgdorferi* (the spirochete causing Lyme disease) and development of cutaneous B-cell non-Hodgkin's lymphoma (CBCL). ***Methods:*** We did a correlation analysis of CBCL and Lyme disease using data from the Surveillance, Epidemiology and End Results program and from the Centers for Disease Control and Prevention. ***Results:*** We could not demonstrate a geographic correlation between incidence rates of Lyme disease and CBCL. ***Conclusion:*** This observation suggests that infection with *B. burgdorferi* is not a major risk factor for CBCL in the USA.

Introduction

The spirochete *Borrelia burgdorferi* has been suggested as a potential causal agent in primary cutaneous B-cell non-Hodgkin's lymphoma (CBCL) [1]. Most infections with *B. burgdorferi* remain subclinical, but when symptomatic, typical manifestations include acute and chronic skin rashes, arthritis and various neurologic deficits (e.g. facial nerve palsy and meningism). This clinical picture is commonly referred to as Lyme disease [2]. In some cases *B. burgdorferi* induces chronic inflammation of the skin with dense lymphocytic infiltration followed by atrophic changes known as chronic atrophic acrodermatitis [3]. Foreign agents, such as tattoo dyes and infections, may induce benign lymphoproliferative reactions in the skin that, histologically, resemble cutaneous lymphomas [4]. Such cutaneous pseudolymphomas are initially oligo- or polyclonal, but may upon continuous stimulation become monoclonal, and it is possible that, in rare instances, CBCL may ultimately develop through mechanisms similar to those described for other B-cell lymphomas [5]. There is some evidence to suggest that *B. burgdorferi* may be associated with CBCL. First, several patients with chronic atrophic acrodermatitis followed by CBCL have been reported in the literature [6]. Second, a German study found serological evidence of *B. burgdorferi* infection in all of 4 CBCL patients examined [7]. Finally, Cerroni et al. [1] have recently demonstrated DNA from *B. burgdorferi* in 9 (18%) of 50 CBCLs in Graz, Austria. In contrast to these European findings, however, *B. burgdorferi* could not be demonstrated with immunohistochemical techniques in a series of 5 American cutaneous immunocytoma patients [8]. The present investigation was undertaken to assess temporal changes in the incidence of CBCL in the USA and to determine whether recent incidence patterns of Lyme disease in the USA correlate geographically with incidence rates of CBCL.

Materials and Methods

Using data from the Surveillance, Epidemiology and End Results program [9], we calculated age-standardized (US population 1970) incidence rates of CBCL among white people in the USA for the period 1973–1996. According to the International Classification of Disease, second edition, we considered a case to be CBCL if the anatomical site was between 440 and 449 (skin) and histology was 9590–9595, 9670–9698 or 9711–9714 (non-Hodgkin's lymphoma except mycosis fungoides, Sézary syndrome and other T-cell lymphomas). For the correlation analysis we calculated age-standardized incidence rates of CBCL for the period 1992–1996 in 11 geographic areas: San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, Los Angeles and San José-Monterey. Incidence rates of Lyme disease for these 11 geographic areas were obtained from the Centers for Disease Control and Prevention [10] and were used to construct 11 pairs of incidence rates of CBCL and Lyme disease. The correlation between rates was assessed by Spearman's rank correlation test [11].

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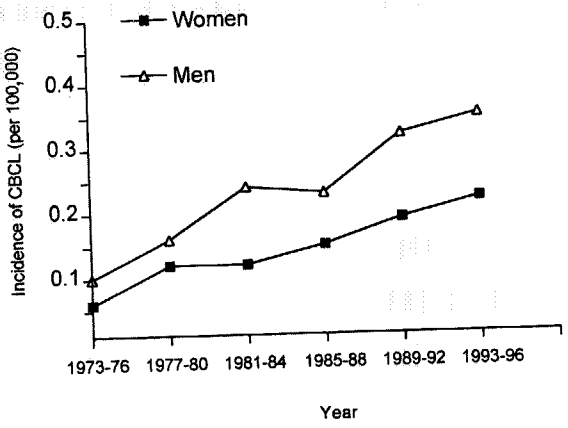

Fig. 1. Age-standardized (US population 1970) incidence rates of CBCL in the USA, 1973–1996.

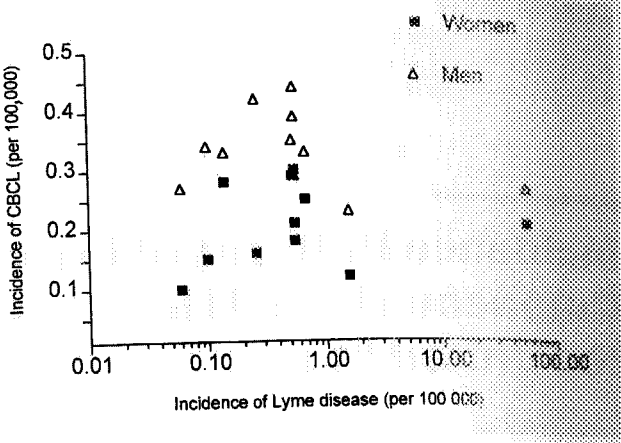

Fig. 2. Incidence rates of CBCL by incidence rates of Lyme disease in 11 geographic areas of the USA.

Results

Based on a total of 940 cases of CBCL (519 men and 421 women), the age-standardized incidence of CBCL increased considerably during the 24-year study period, i.e. from 0.10 to 0.35 per 100,000 in men and from 0.06 to 0.22 per 100,000 in women between 1973–1976 and 1993–1996 (fig. 1). This corresponds to an annual increase in incidence of 6.3% in men and 5.5% in women (linear regression: $p_{trend} < 0.05$ for each sex). The reported incidence of Lyme disease in the USA has increased steadily since 1991, when a standard case definition for Lyme disease was first introduced, ranging from approximately 3.6 per 100,000 population in 1991 to 6.4 per 100,000 population in 1998. Age-standardized rates for CBCL did not correlate with incidence rates of Lyme disease in women ($r = 0.23$, $p = 0.50$) or in men ($r = -0.26$, $p = 0.44$; fig. 2).

Discussion

The present analysis failed to demonstrate a correlation between incidences of Lyme disease and CBCL. The underlying true incidence of infection with *B. burgdorferi* is not known, but the incidence of reported Lyme disease has increased considerably over the past decade and varies remarkably (up to several hundredfold) between endemic and nonendemic areas in the USA [10]. Presumably, the increase in Lyme disease results in part from increased recognition and monitoring since *B. burgdorferi* was established as the causal agent in 1982 [12]. Additionally some geographic variation in the completeness of reporting of Lyme disease cannot be ruled out. However, the proportional increases in reported rates of Lyme disease in different geographic regions were largely similar, suggesting that they are correlated with the true rates of infection with *B. burgdorferi*. Consequently, the lack of a geographic correlation between reported incidence rates of Lyme disease and CBCL suggests that the strains of *B. burgdorferi* that prevail in the northeastern, mid-Atlantic and upper north-central regions of the USA are not an important cause of CBCL. Earlier reports of an association between *B. burgdorferi* and CBCL have all been of European origin. Therefore strain variability may explain differences in *Borrelia*-associated disease between North America and Europe [13].

References

1 Cerroni L, Zochling N, Putz B, Kerl H: Infection by *Borrelia burgdorferi* and cutaneous B-cell lymphoma. J Cutan Pathol 1997;24:457–461.

2 Steere AC: Lyme disease. N Engl J Med 1989; 321:586–596.

3 Asbrink E, Hovmark A, Hederstedt B: The spirochetal etiology of acrodermatitis chronica atrophicans Herxheimer. Acta Derm Venereol 1984;64:506–512.

4 Ploysangam T, Breneman DL, Mutasim DF: Cutaneous pseudolymphomas. J Am Acad Dermatol 1998;38:877–895.

5 Slater DN: MALT and SALT: The clue to cutaneous B-cell lymphoproliferative disease. Br J Dermatol 1994;131:557–561.

6 Garbe C, Stein H, Gollnick H, Taud W, Orfanos CE: Kutanes B-Zell-Lymphom bei chronischer *Borrelia-burgdorferi*-Infektion: Bericht über zwei Fälle und Literaturübersicht (in German). Hautarzt 1988;39:717–726.

7 Garbe C, Stein H, Dienemann D, Orfanos CE: *Borrelia burgdorferi*-associated cutaneous B cell lymphoma: Clinical and immunohistologic characterization of four cases. J Am Acad Dermatol 1991;24:584–590.

8 LeBoit PE, McNutt NS, Reed JA, Jacobson M, Weiss LM: Primary cutaneous immunocytoma: A B-cell lymphoma that can easily be mistaken for cutaneous lymphoid hyperplasia. Am J Surg Pathol 1994;18:969–978.

9 Ries LAG, Kosary CL, Hankey BF, Miller BA, Edwards BK: SEER Cancer Statistics Review. Bethesda, National Cancer Institute, 1999.

10 Centers for Disease Control and Prevention: Reported Cases of Lyme Disease by State, 1989–1998. http://www.cdc.gov/ncidod/dvbid/lymeepi.htm.

11 Altman DG: Rank Correlation; in Altman DG (ed): Practical Statistics for Medical Research, ed 12. London, Chapman & Hall, 1993, pp 285–288.

12 Burgdorfer W, Barbour AG, Hayes SF, Benach JL, Grunwaldt E, Davis JP: Lyme disease – A tick-borne spirochetosis? Science 1982;216: 1317–1319.

13 Nadelman RB, Wormser GP: Lyme borreliosis. Lancet 1998;352:557–565.